

Amendment to the Claims

1. (Withdrawn) A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to a secreted protein gene;
 - (b) a second polynucleotide sequence homologous to the secreted protein gene; and
 - (c) a selectable marker.
2. (Withdrawn) The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. (Withdrawn) A method of producing a secreted protein gene targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a secreted protein gene;
 - (b) providing a second polynucleotide sequence homologous to the secreted protein gene;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. (Withdrawn) A method of producing a secreted protein gene targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a secreted protein gene and a second sequence homologous to a second region of a secreted protein gene;
 - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. (Canceled)
6. (Canceled)
7. (Canceled)
8. (Currently amended) A ~~non-human transgenic mouse animal~~ whose genome comprises a null endogenous comprising a disruption in a secreted protein allele, wherein said endogenous allele encodes for mRNA comprising the mouse homologue of SEQ ID NO:1 gene.
9. (Currently amended) A cell or tissue derived from the ~~mouse~~ non-human transgenic animal of claim 8.

10. (Currently amended) A method of producing ~~a the~~ transgenic mouse ~~of claim 8 comprising a~~ disruption in a secreted protein encoding gene, the method comprising:
- (a) introducing ~~a the~~ targeting construct capable of introducing a disruption into the mouse homolog of SEQ ID NO:1 ~~of claim 1~~ into a mouse embryonic stem cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse.
11. (Withdrawn) A method of identifying an agent that modulates the expression of a secreted protein encoding gene, the method comprising:
- (a) providing a non-human transgenic animal comprising a disruption in the secreted protein encoding gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the expression of the secreted protein encoding gene in the non-human transgenic animal is modulated.
12. (Withdrawn) A method of identifying an agent that modulates the function of a secreted protein encoded by a secreted protein encoding gene, the method comprising:
- (a) providing a non-human transgenic animal comprising a disruption in the secreted protein encoding gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the function of the secreted protein in the non-human transgenic animal is modulated.
13. (Withdrawn) A method of identifying an agent that modulates the expression of a secreted protein gene, the method comprising:
- (a) providing a cell comprising a disruption in the secreted protein gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether expression of the secreted protein gene is modulated.
14. (Withdrawn) A method of identifying an agent that modulates the function of a secreted protein gene, the method comprising:
- (a) providing a cell comprising a disruption in the secreted protein gene;

- (b) contacting the cell with an agent; and
 - (c) determining whether the function of the secreted protein gene is modulated.
15. (Withdrawn) An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.
16. (Canceled)
17. (Canceled)
18. (Currently amended) The transgenic mouse of claim 189, wherein the mouse exhibits an anti-depressive condition ~~is characterized by decreased time spent immobile in a tail suspension test, relative to a wild-type mouse.~~
19. (Canceled)
20. (Canceled)
21. (Currently amended) A method of identifying an agent that has an effect on depression, the method comprising;
- (a) administering an agent to ~~the~~ a transgenic mouse of claim 8 ~~comprising a disruption in a secreted protein gene;~~ and
 - (b) determining whether the agent has an effect on depression, wherein the effect on depression is measured in a behavioral test.
22. (Withdrawn) A method of identifying an agent that modulates expression of a secreted protein gene, the method comprising:
- (a) administering an agent to a transgenic mouse comprising a disruption in the secreted protein gene; and
 - (b) determining whether the agent modulates expression of the secreted protein gene in the transgenic mouse, wherein the agent has an effect on an anti-depressive condition.
23. (Currently amended) A method of identifying an agent that modulates a behavior associated with a disruption in a secreted protein gene, the method comprising:
- (a) administering an agent to ~~the~~ a transgenic mouse of claim 8 ~~comprising a disruption in the secreted protein gene;~~
 - (b) administering the agent to a wild-type control mouse; and
 - ~~(b)(c)~~ comparing the effect of the agent on behavior in the transgenic mouse and the wild-type; thereby determining whether the agent has an effect on behavior ~~depression, wherein the effect on depression is measured in a behavioral test.~~

24. (Withdrawn) A method of identifying an agent that modulates the function of a secreted protein gene encoding a secreted protein, the method comprising:
- (a) providing a cell comprising a disruption in the secreted protein gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the agent modulates the function of the secreted protein gene, wherein the agent modulates a phenotype associated with a disruption in the secreted protein gene.
25. (Withdrawn) The method of claim 25, wherein the phenotype comprises anti-depressant behavior.
26. (Withdrawn) A method of identifying an agent that has an effect on depression, the method comprising:
- (a) providing a secreted protein encoded by a secreted protein gene;
 - (b) contacting the secreted protein with an agent; and
 - (c) determining if the agent modulates the function of the secreted protein.
27. (Withdrawn) A method of identifying an agent that has an effect on depression, the method comprising:
- (a) providing a cell expressing a secreted protein gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the agent affects the function of the secreted protein.
28. (Withdrawn) A method of identifying an agent that has an effect on depression, the method comprising:
- (a) providing a cell overexpressing a secreted protein gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the agent affects the expression of the secreted protein gene.
29. (Withdrawn) The method of claim 28, wherein the agent decreases the expression of the secreted protein gene.
30. (Withdrawn) An agent identified by the method of claim 26, claim 27, or claim 28.
31. (Withdrawn) A method of treating depression, or ameliorating symptoms associated therewith, the method comprising administering to a patient in need a therapeutically effective amount of an agent that modulates expression of a secreted protein gene.

32. (Withdrawn) A method of treating depression, or ameliorating symptoms associated therewith, in a patient in need, the method comprising administering to a patient in need a therapeutically effective amount of an agent that inhibits the expression or activity of a protein encoded by a secreted protein gene.
33. (Withdrawn) A method of treating depression, or ameliorating symptoms associated therewith, in a patient in need, the method comprising administering an agent that modulates the activity of a secreted protein encoded by a secreted protein gene.
34. (Withdrawn) The method of claim 33, wherein the agent is an antagonist of the secreted protein.
35. (Withdrawn) The method of claim 34, wherein the antagonist is an antibody.
36. (New) The transgenic mouse of claim 8, wherein the mouse is heterozygous for said null allele.
37. (New) The transgenic mouse of claim 8, wherein the mouse is homozygous for said null allele.
38. (New) The transgenic mouse of claim 8, wherein the null allele comprises a gene encoding a selectable marker.
39. (New) The transgenic mouse of claim 38, wherein the gene encoding the selectable marker is *Neo^r*.